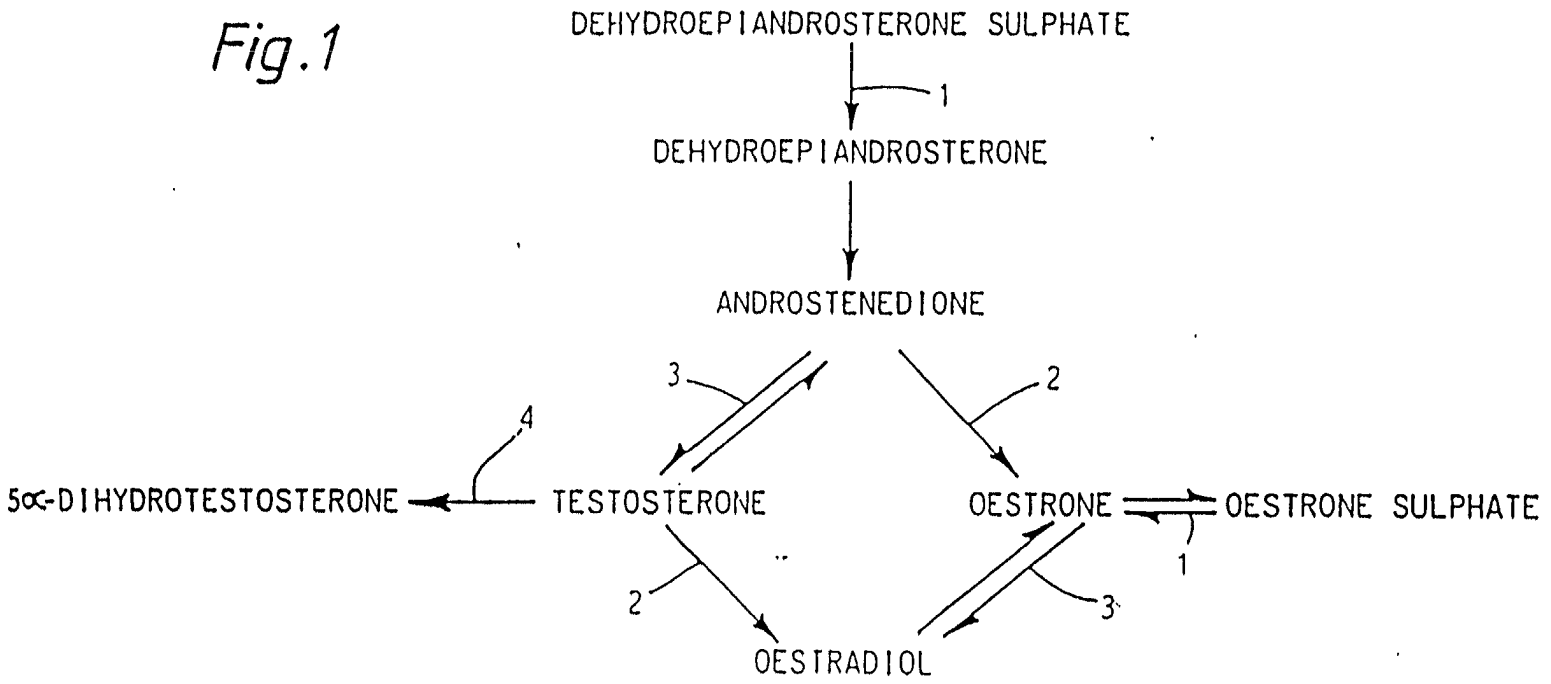
Fig.1



KEY ENZYMES IN STEROIDOGENESIS:-

1. SULPHATASE 2. AROMATASE 3. DEHYDROGENASE 4. 5∝REDUCTASE

Fig. 2

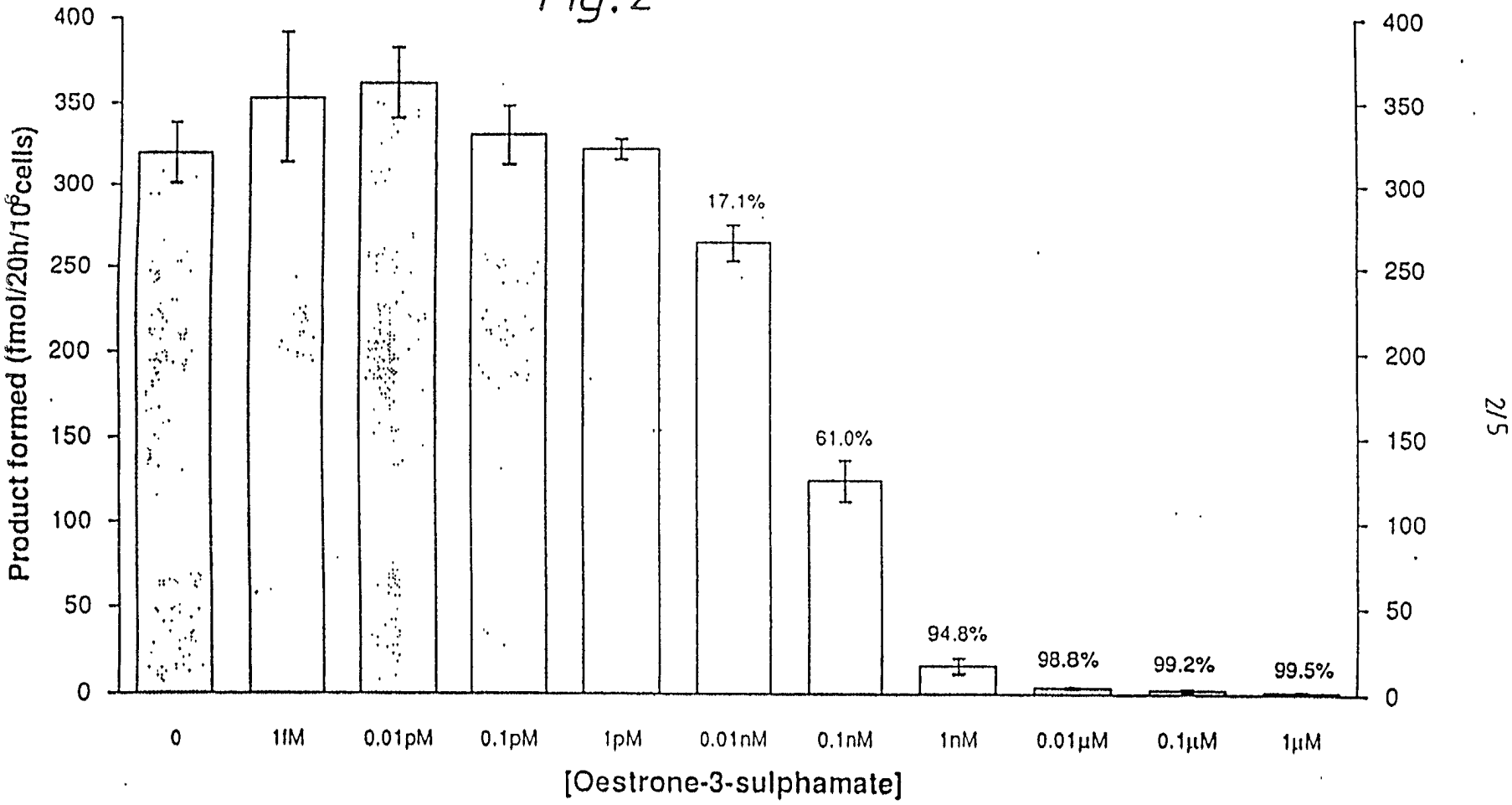

Product formed (fmol/20h/10^6cells)
400
350
300
250
200
150
100
50
0
17.1%
61.0%
94.8%
98.8%
99.2%
99.5%
0
1fM
0.01pM
0.1pM
1pM
0.01nM
0.1nM
1nM
0.01µM
0.1µM
1µM
[Oestrone-3-sulphamate]

Fig. 3

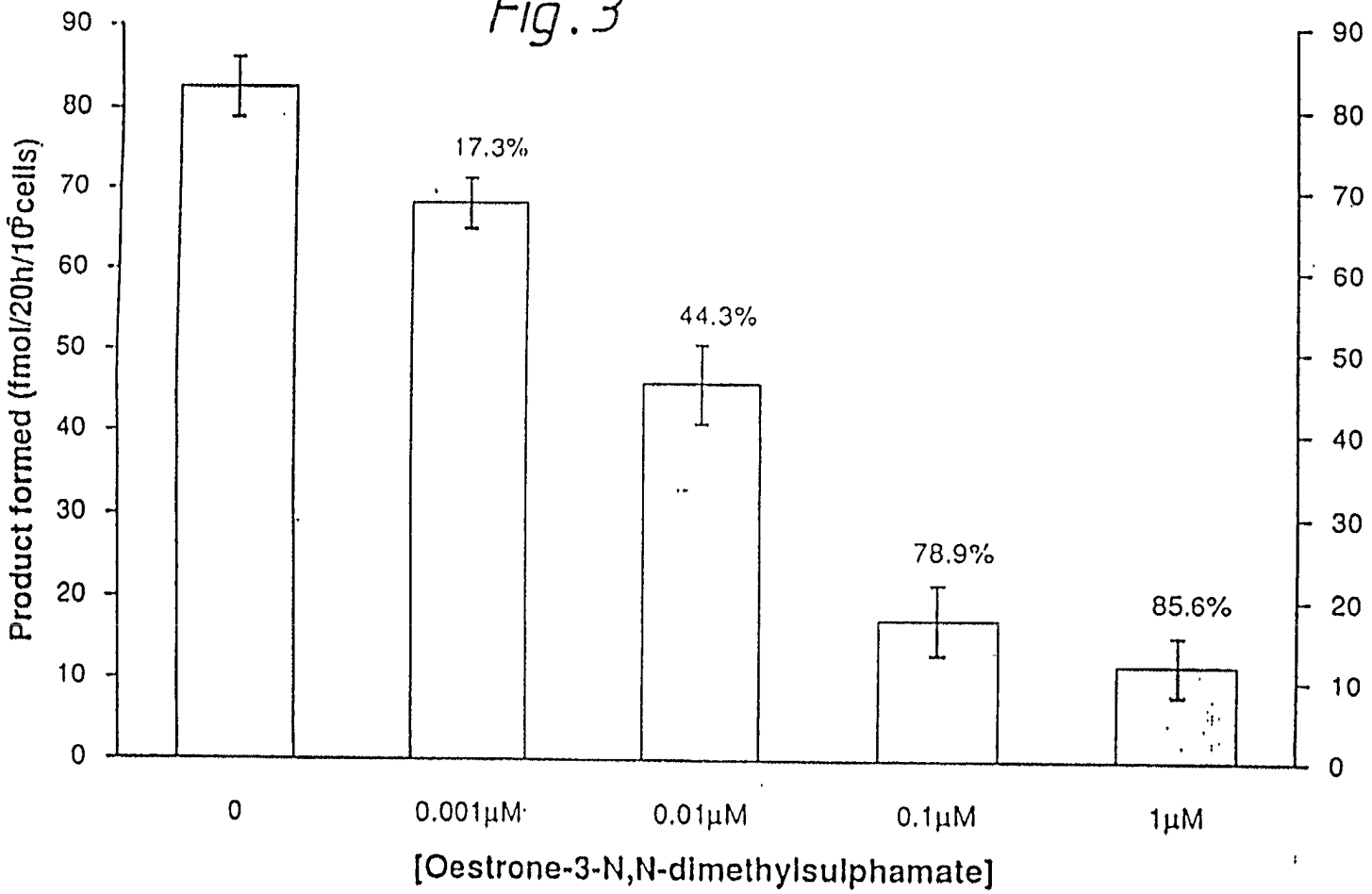


Fig. 4

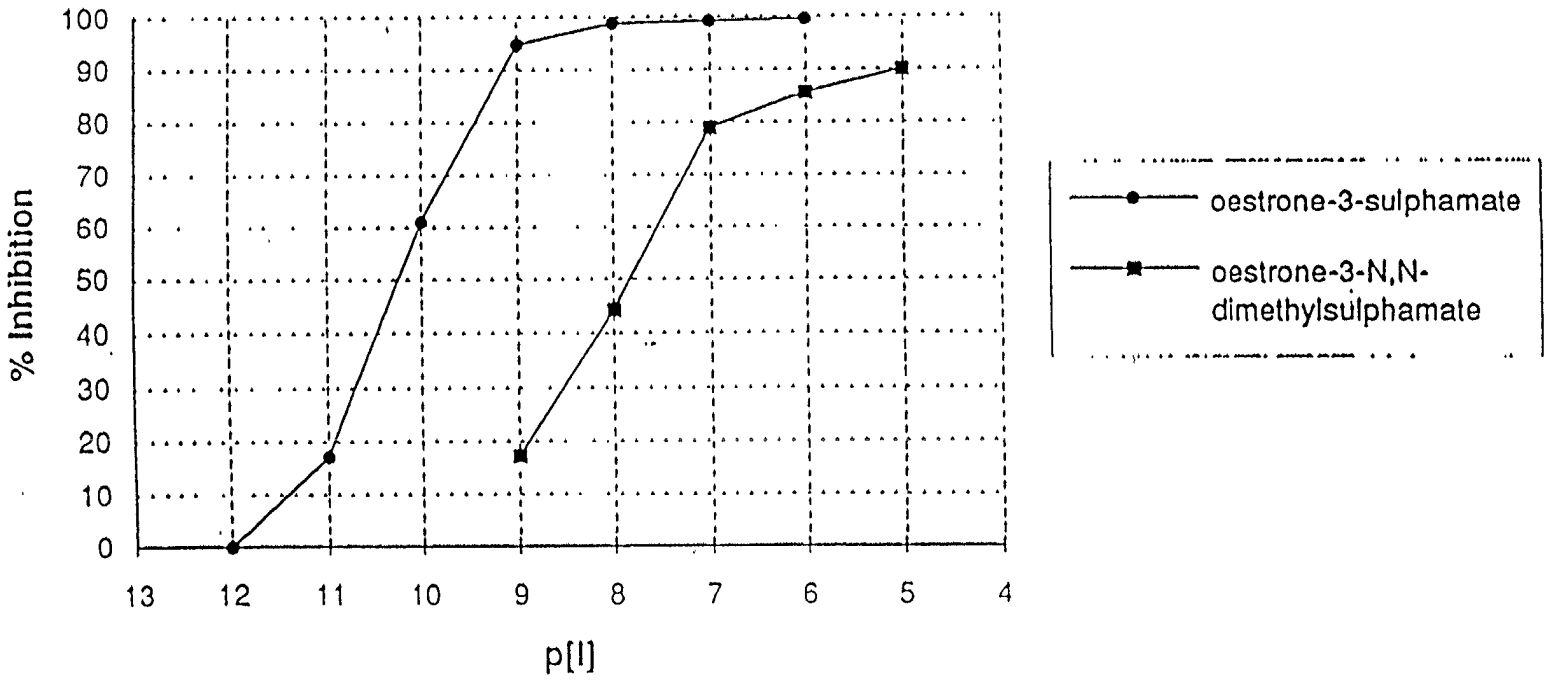
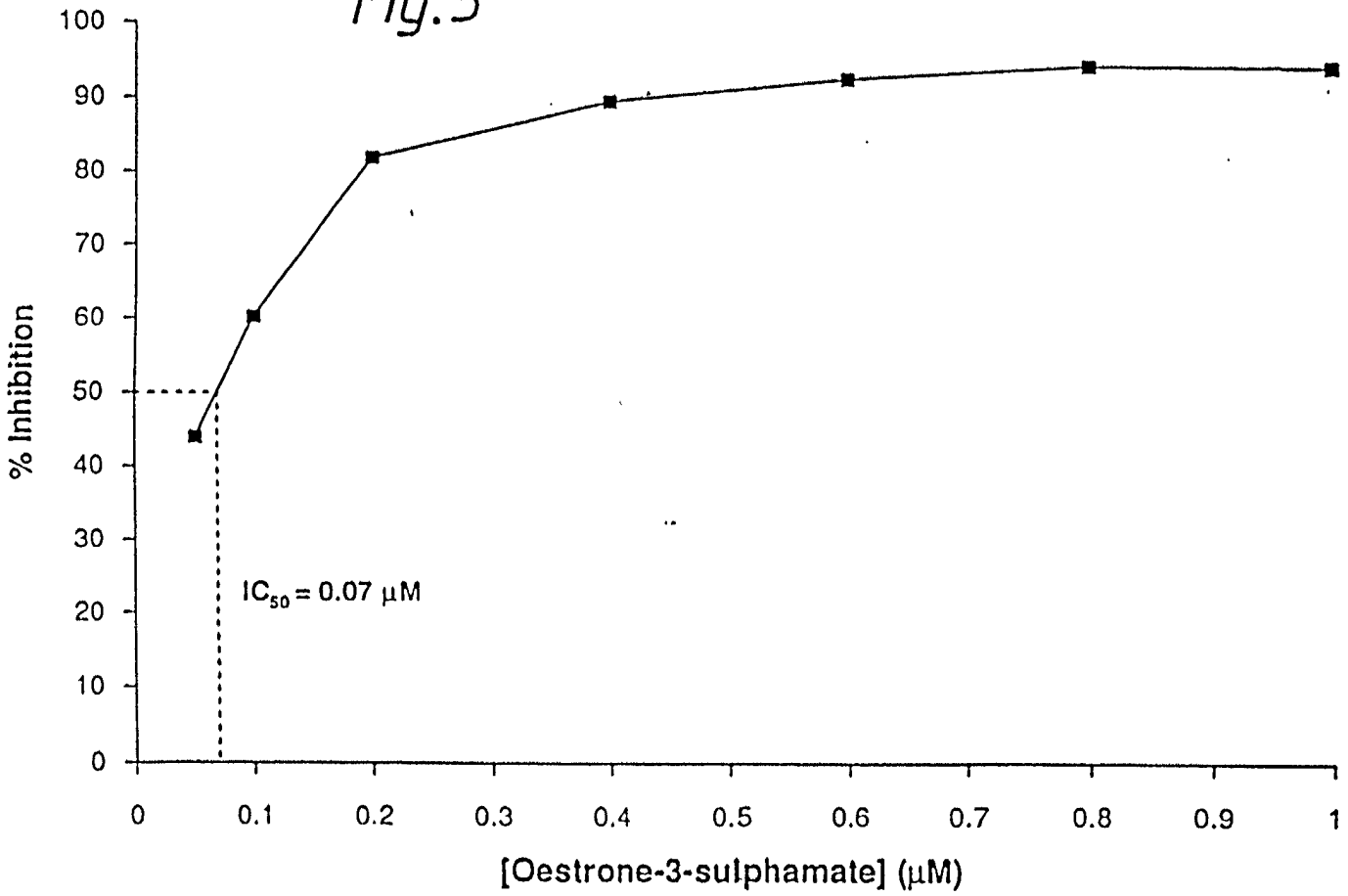
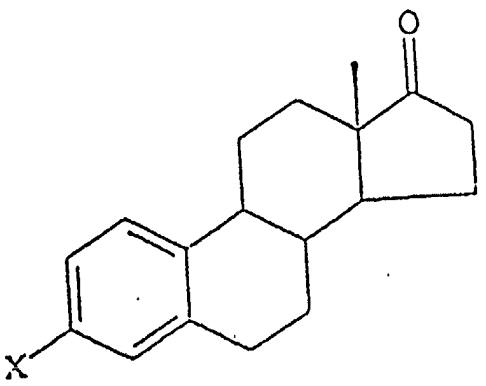

% Inhibition
100
90
80
70
60
50
40
30
20
10
0
13
12
11
10
9
8
7
6
5
4
p[I]
oestrone-3-sulphamate
oestrone-3-N,N-dimethylsulphamate

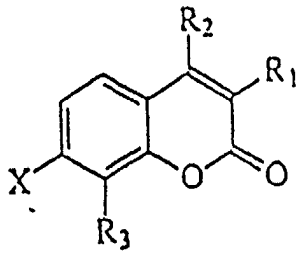
Fig.5


100
90
80
70
60
50
40
30
20
10
0
% Inhibition
IC50 = 0.07 µM
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
[Oestrone-3-sulphamate] (µM)



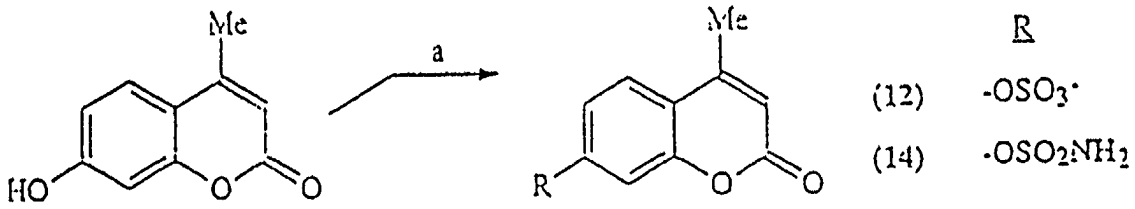
	X
(1)	-OH
(2)	$-OSO_3^-$
(3)	$-OSO_2NH_2$
(4)	$-NHSO_2NH_2$
(5)	$-SSO_2NH_2$

FIG. 6



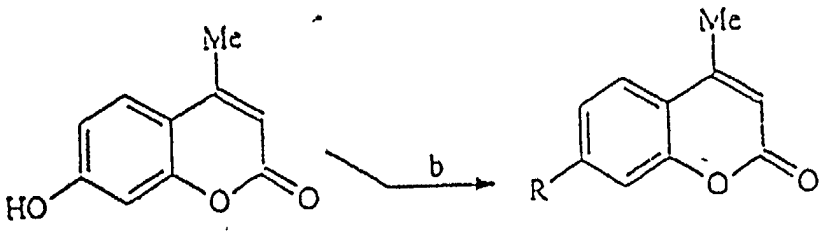
	X	R1	R2	R3
(11)	-OH	H	H	H
(12)	$-OSO_3^-$	H	CH_3	H
(13)	$-OSO_2NH_2$	H	H	H
(14)	$-OSO_2NH_2$	H	CH_3	H
(15)	$-OSO_2NH_2$	CH_3	CH_3	CH_3
(16)	$-OSO_2NH_2$	H	CF_3	H

FIG. 7



	R
(12)	$-OSO_3^-$
(14)	$-OSO_2NH_2$

FIG. 8



	R
(12)	$-OSO_3^-$
(14)	$-OSO_2NH_2$

FIG. 9

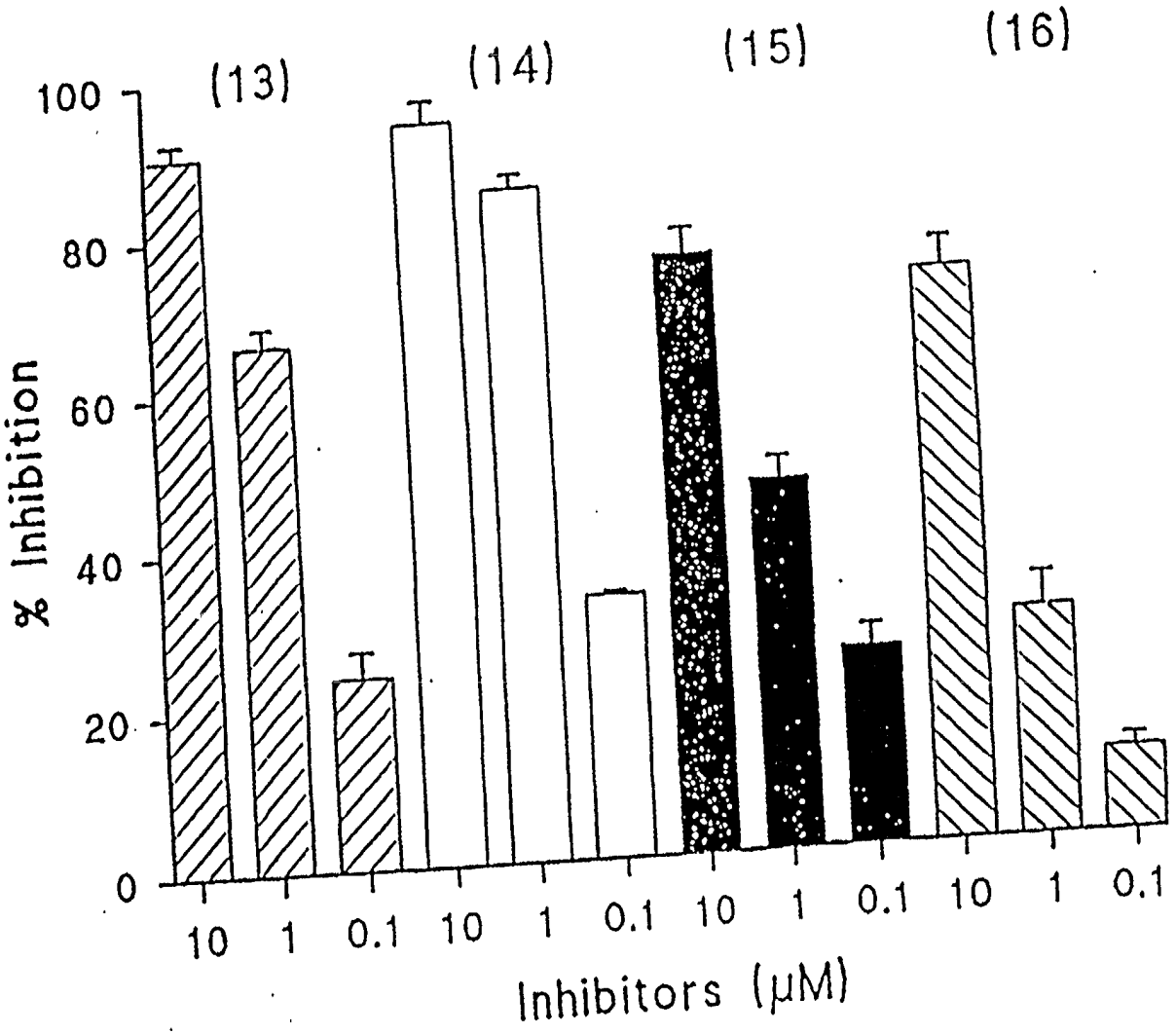


FIG. 10

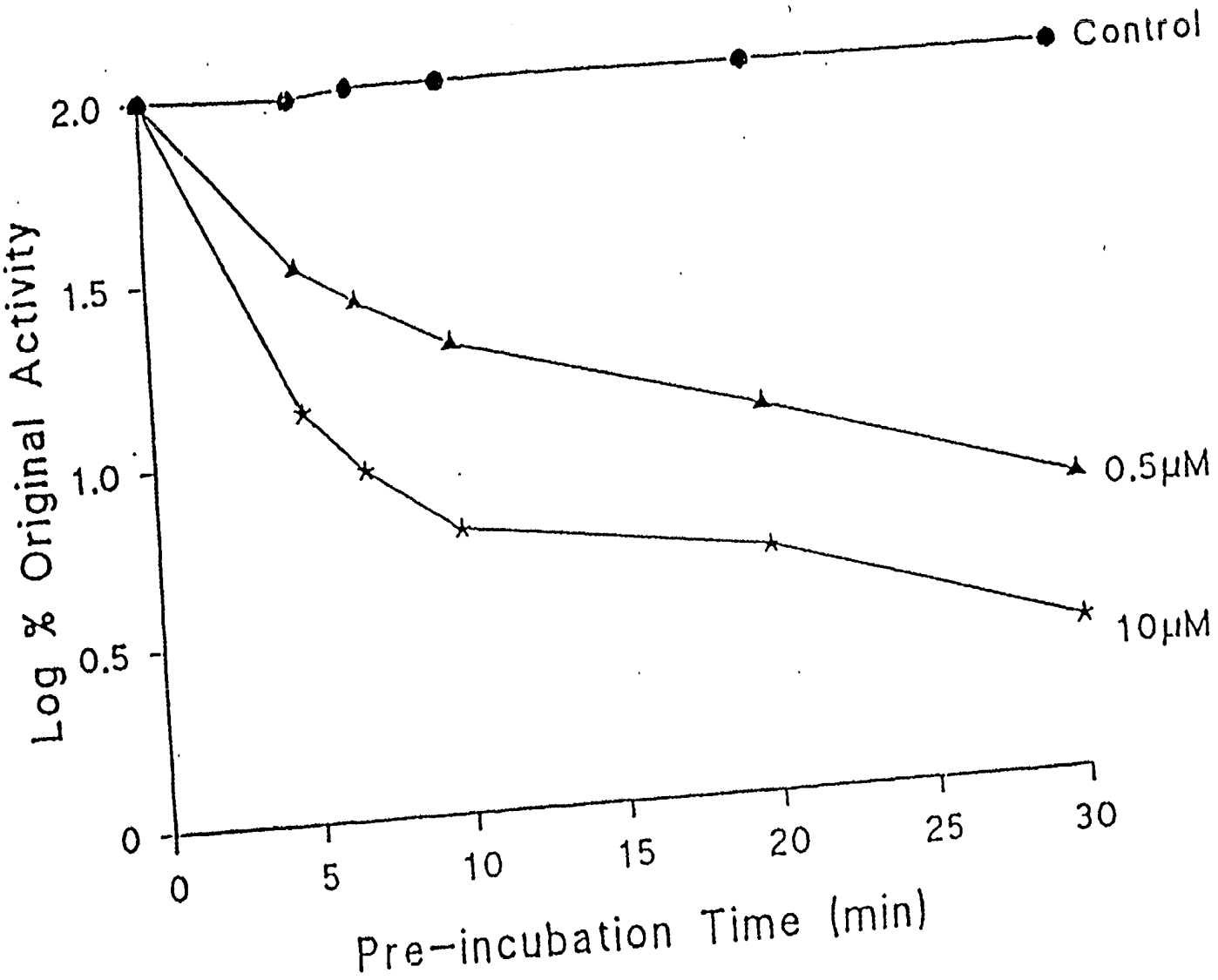


FIG. 11

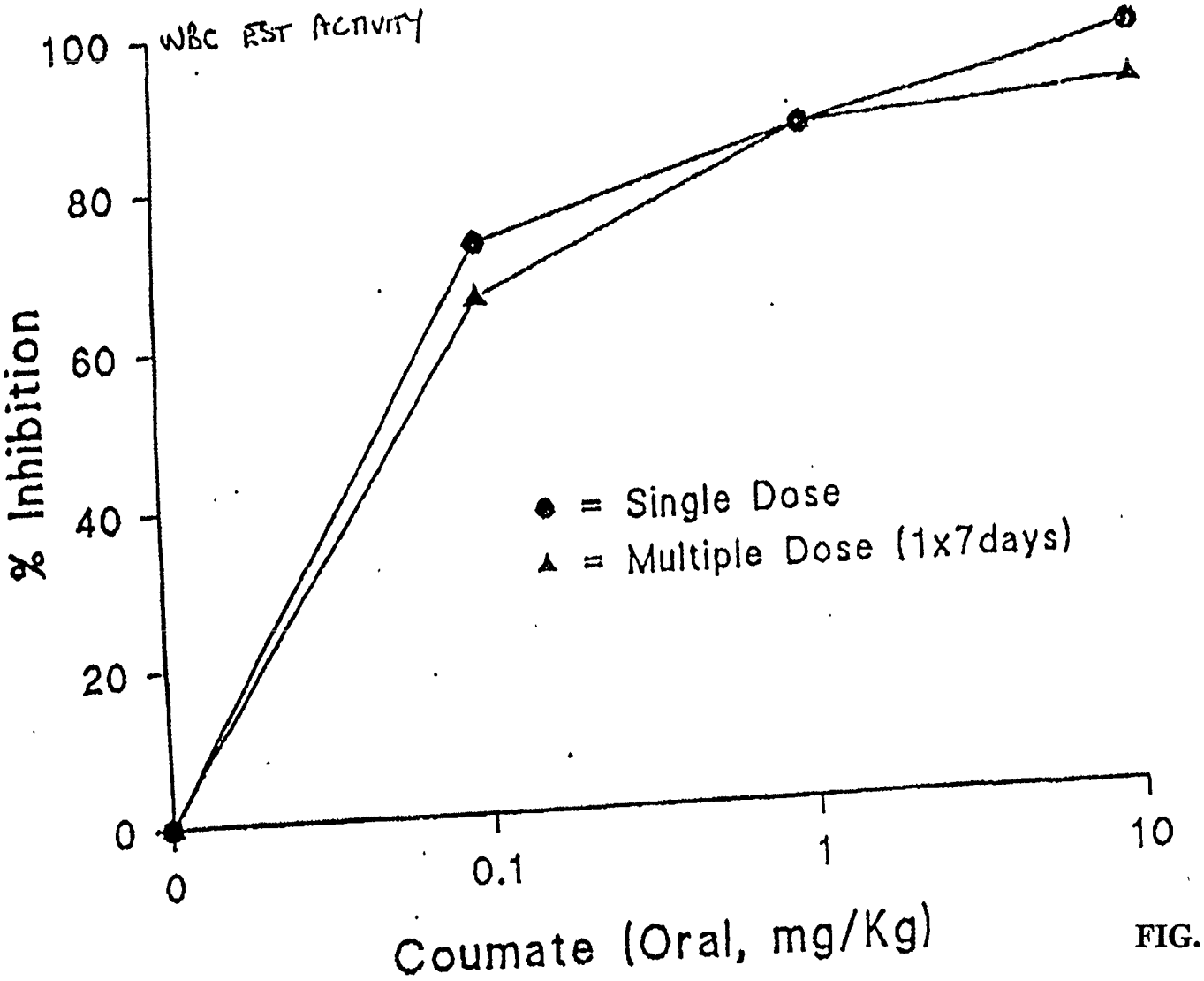
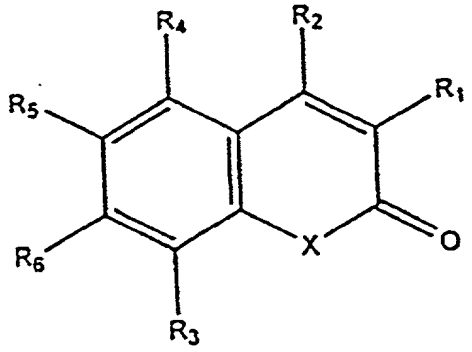
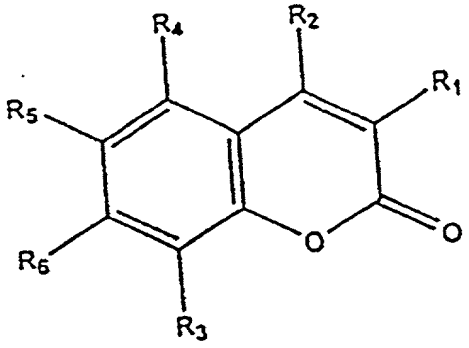

WBC REST ACTIVITY
100
80
60
40
20
0
% Inhibition
● = Single Dose
▲ = Multiple Dose (1x7days)
0
0.1
1
10
Coumate (Oral, mg/Kg)

FIG. 12

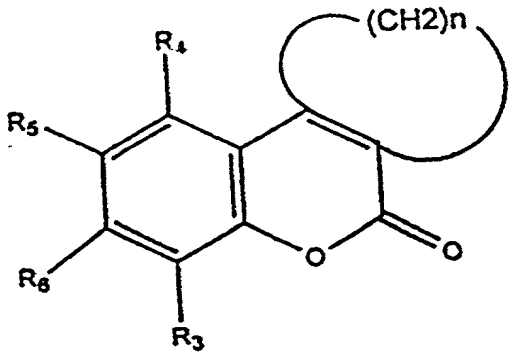
FIG. 13



(A)



(B)



(C)

FIG. 14

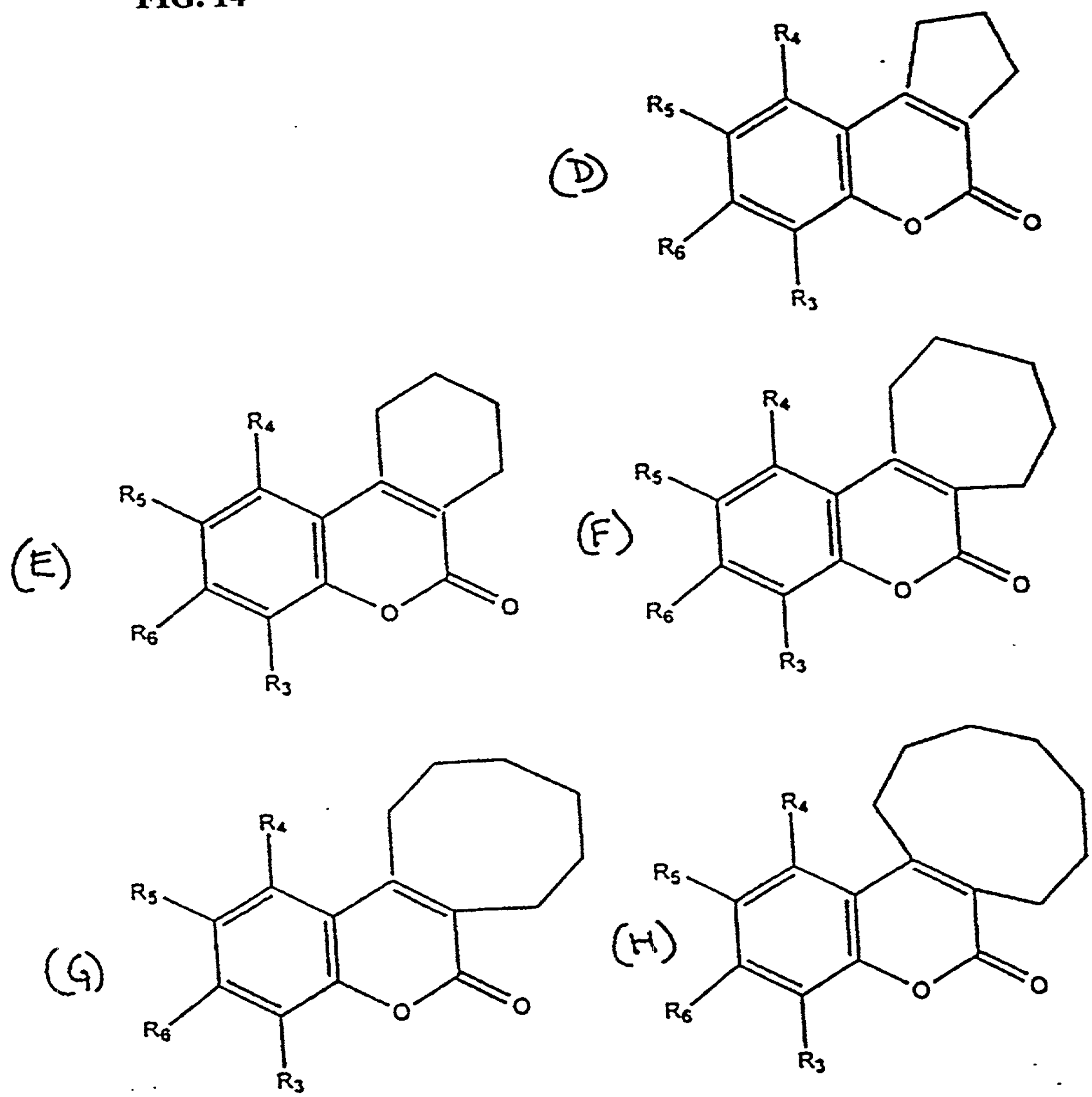
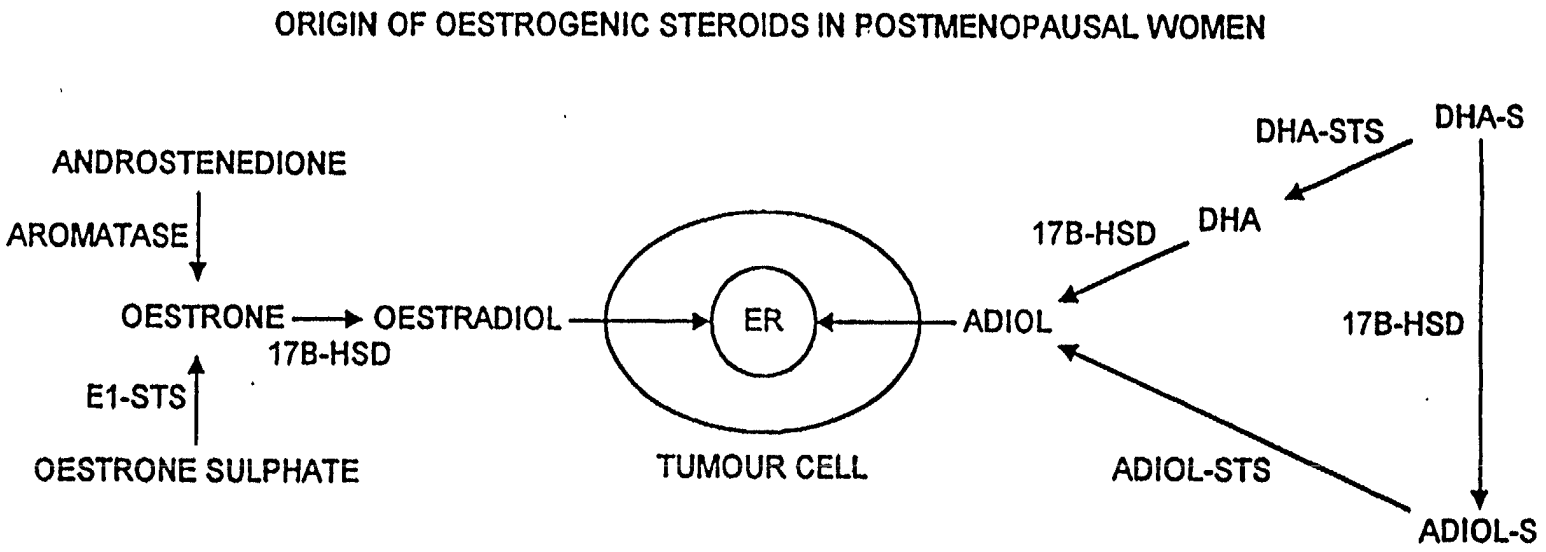
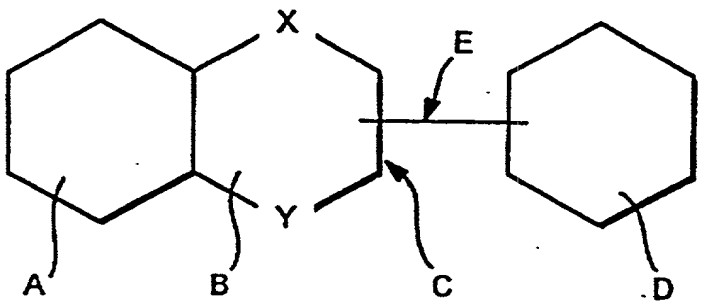


FIG. 15



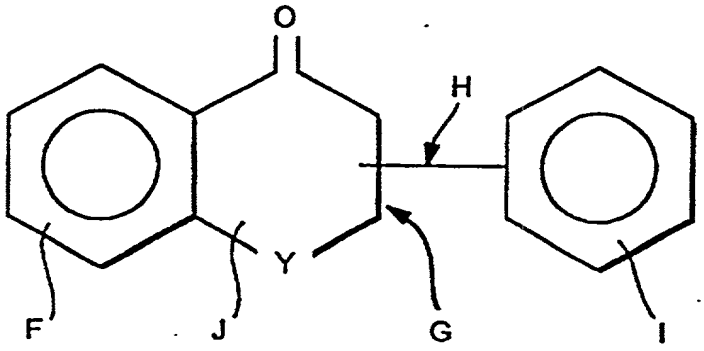
ER=OESTROGEN RECEPTOR, DHA / -S=DEHYDROEPIANDROSTERONE / -SULPHATE, ADIOL=ANDROSTENEDIOL, E1-STS=OESTRONE SULPHATASE, DHA -STS= DHA-SULPHATASE, ADIOL-STS=ADIOL SULPHATASE, 17B-HSD=OESTRADIOL 17B-HYDROXYSTEROID DEHYDROGENASE

FIG. 16a



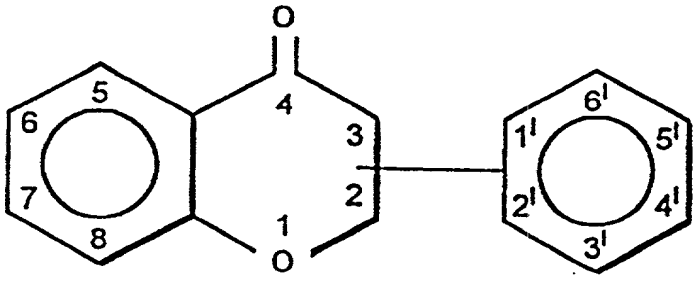
I

FIG. 16b

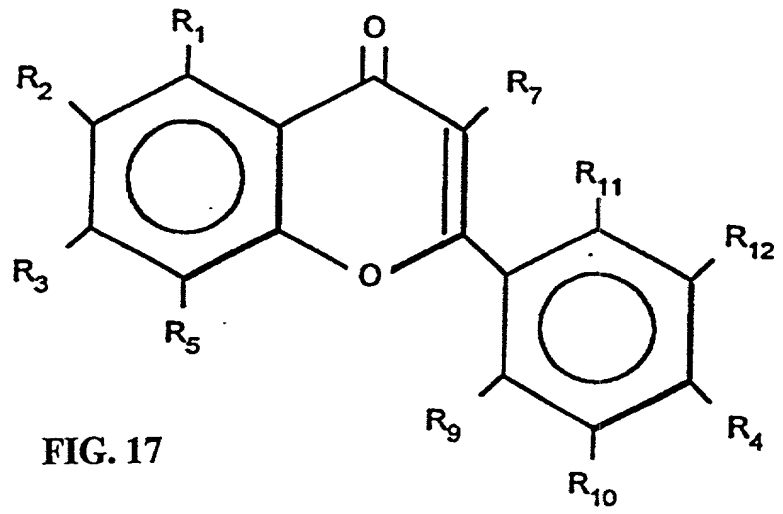


II

FIG. 16c



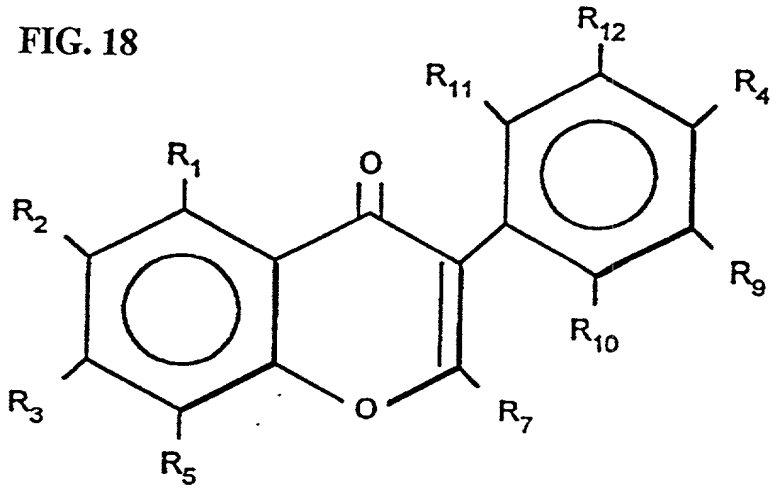
III



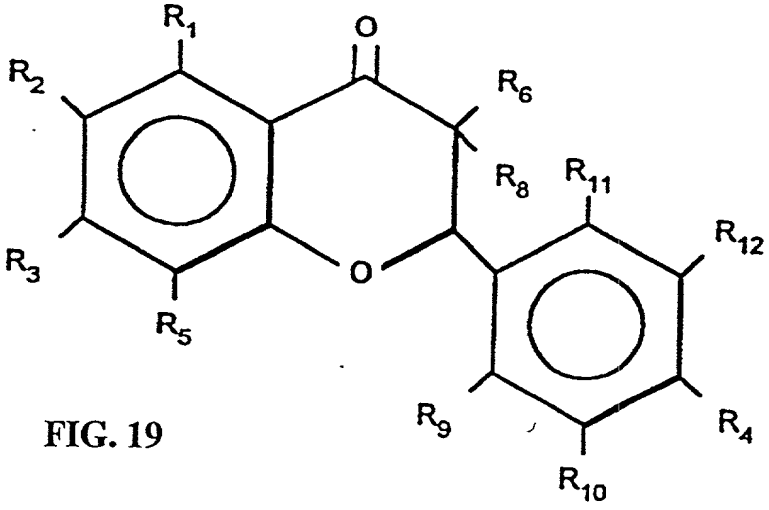
IV

FIG. 17

FIG. 18



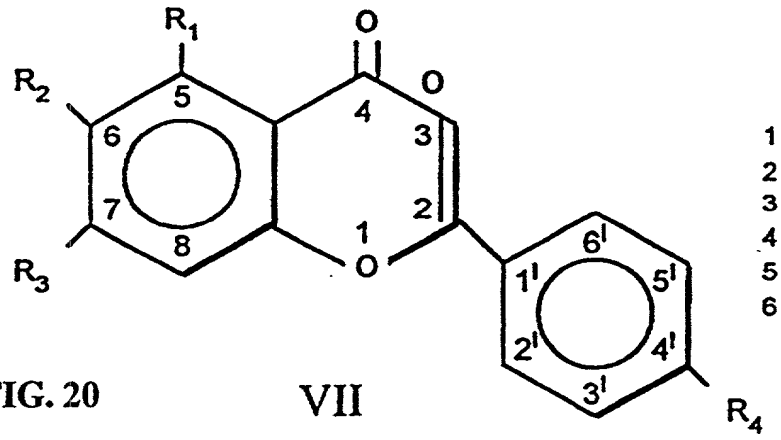
V



VI

FIG. 19

FLAVONES



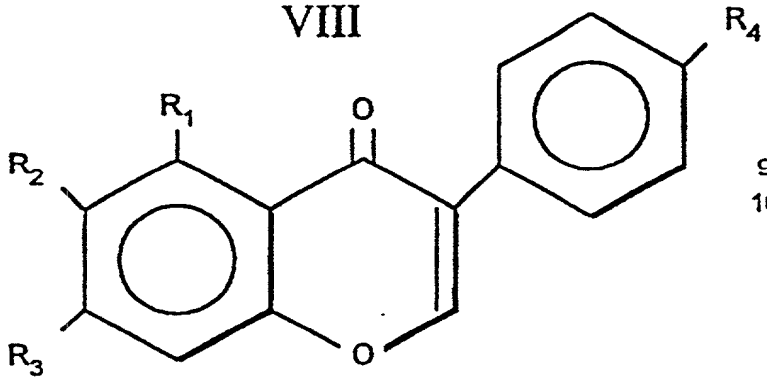
	R_1	R_2	R_3	R_4
1	H	OH	H	H
2	H	OSO_2NH_2	H	H
3	H	H	OH	H
4	H	H	OSO_2NH_2	H
5	OH	H	OH	H
6	OH	H	OSO_2NH_2	H

FIG. 20 VII

ISOFLAVONES

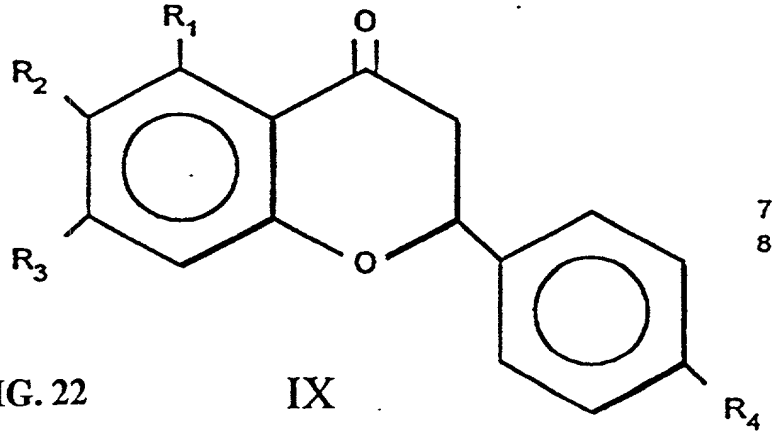
FIG. 21

VIII



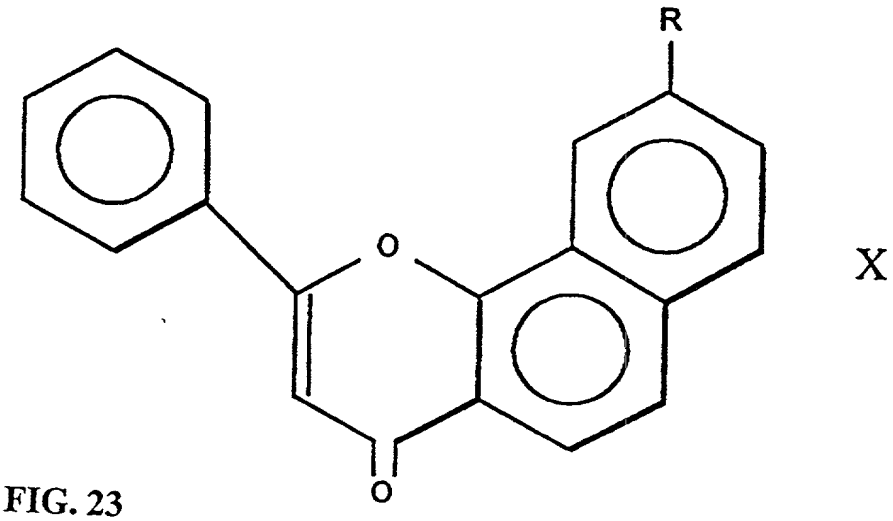
	R_1	R_2	R_3	R_4
9	OH	OH	H	OCH_3
10	OH	H	OSO_2NH_2	OCH_3

FLAVANONES



	R_1	R_2	R_3	R_4
7	OH	H	OH	OH
8	OH	H	OH	OSO_2NH_2

FIG. 22 IX



X

FIG. 23

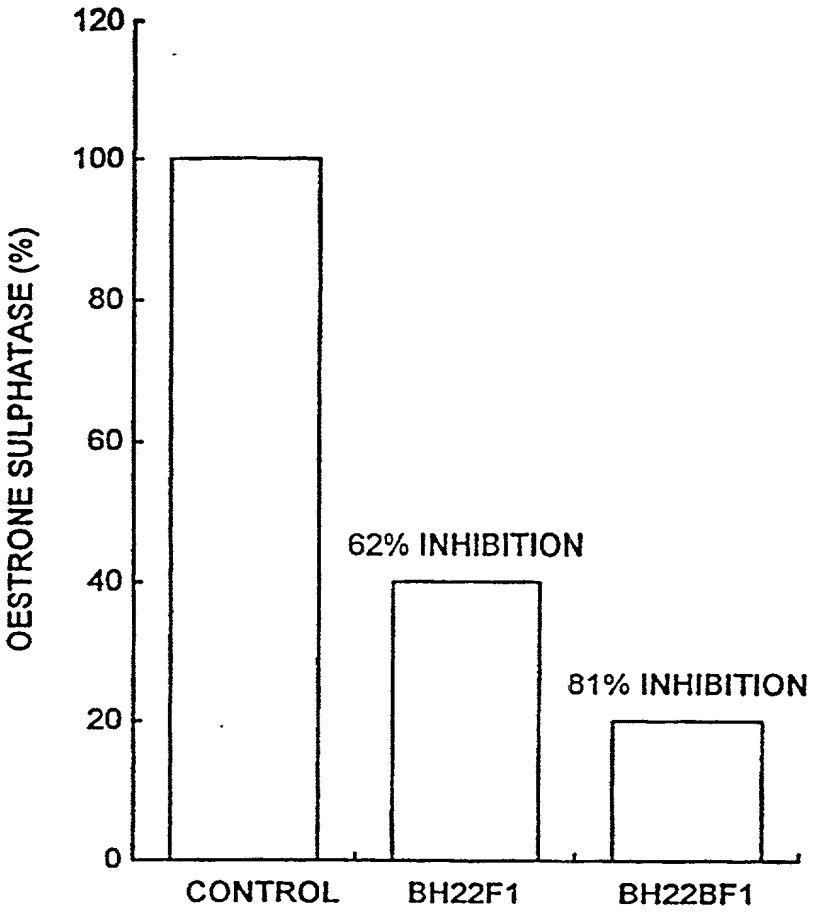
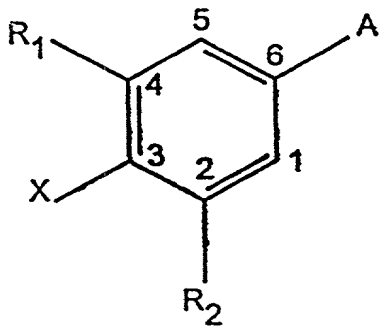

120
100
80
60
40
20
0
OESTRONE SULPHATASE (%)
62% INHIBITION
81% INHIBITION
CONTROL
BH22F1
BH22BF1

FIG. 24

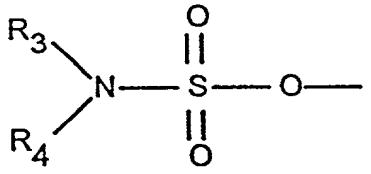
X - B - A I

FIG. 25



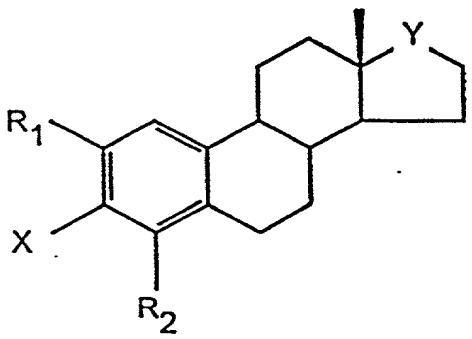
II

FIG. 26



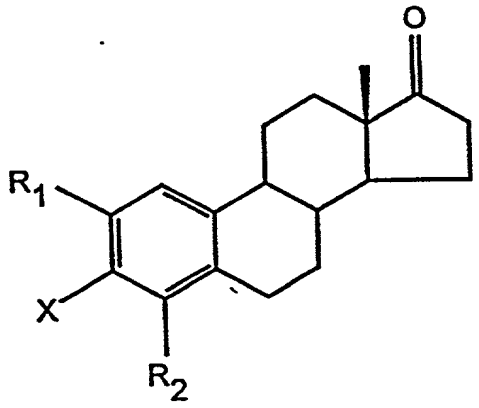
III

FIG. 27



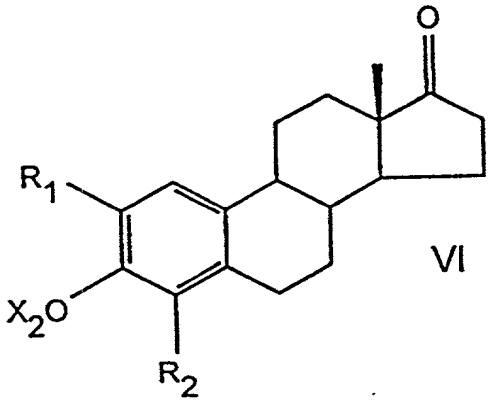
IV

FIG. 28



V

FIG. 29

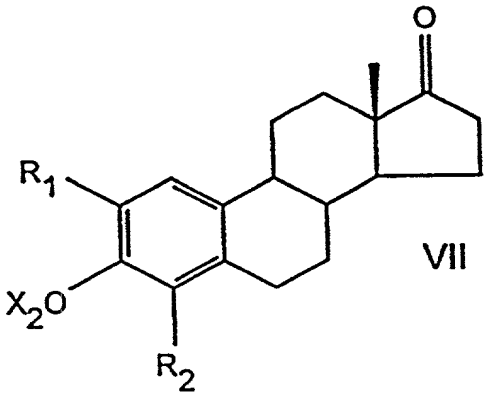


VI

X_2 = - SO_2NH_2

	R_1	R_2
a)	n-$CH_2CH_2CH_3$	H
b)	H	n-$CH_2CH_2CH_3$
c)	n-$CH_2CH_2CH_3$	n-$CH_2CH_2CH_3$

FIG. 30

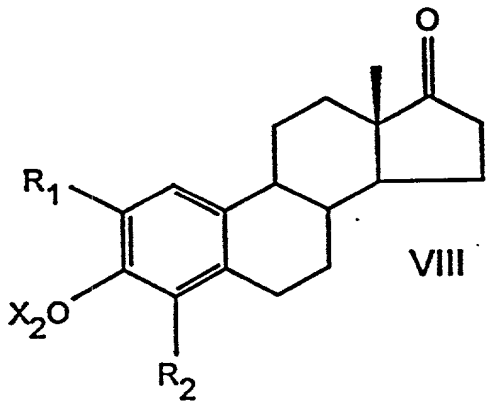


VII

X_2 = - SO_2NH_2

	R_1	R_2
a)	-$CH_2CH=CH_2$	H
b)	H	-$CH_2CH=CH_2$
c)	-$CH_2CH=CH_2$	-$CH_2CH=CH_2$

FIG. 31

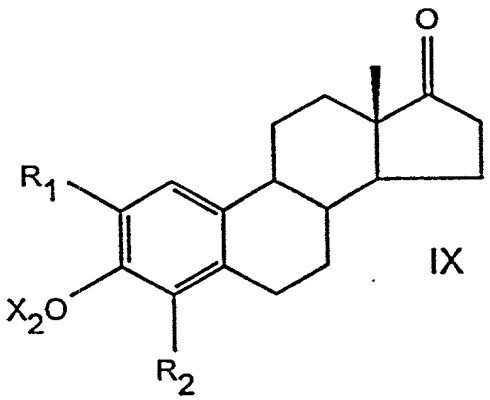


VIII

X_2 = - SO_2NH_2

	R_1	R_2
a)	H_3CO-	H
b)	H	H_3CO-
c)	H_3CO-	H_3CO-

FIG. 32



IX

X_2 = - SO_2NH_2

	R_1	R_2
a)	-NO_2	H
b)	H	-NO_2
c)	-NO_2	-NO_2

FIG. 33

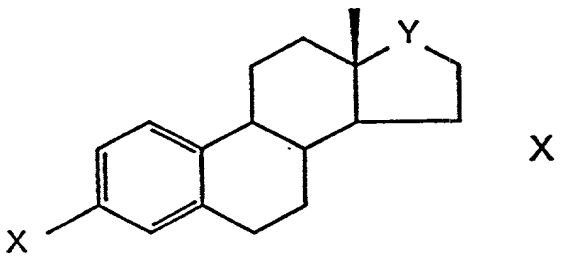


FIG. 34

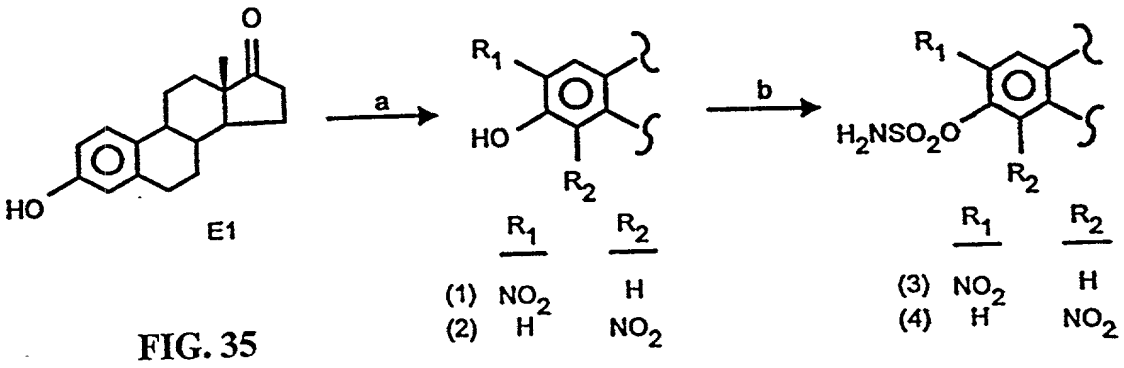


FIG. 35

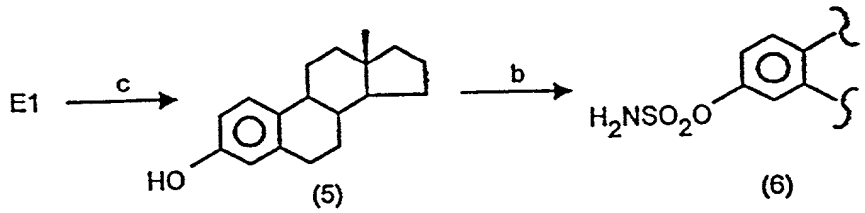


FIG. 36

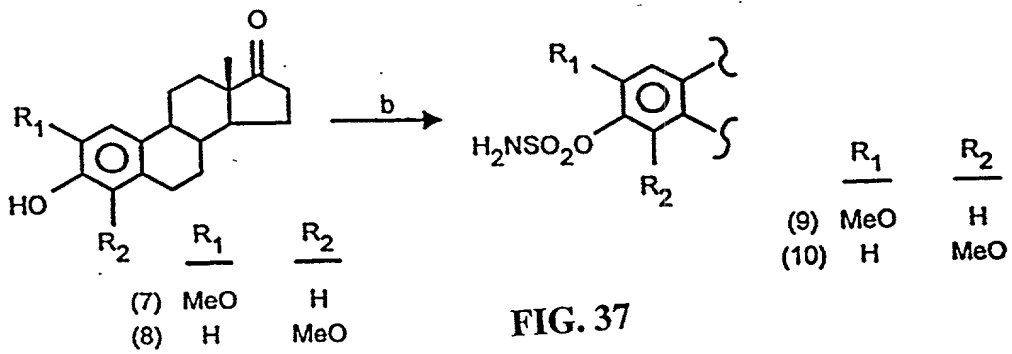
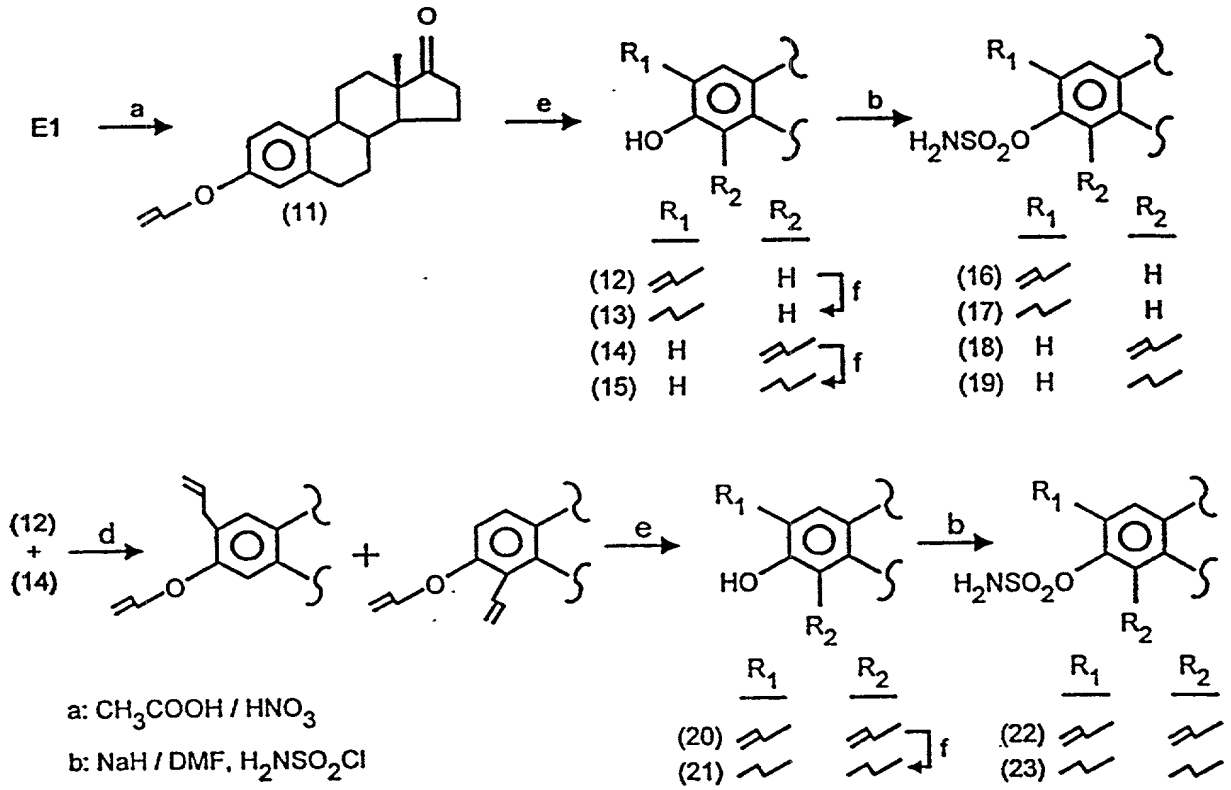


FIG. 37



a: CH_3COOH / HNO_3

b: NaH / DMF, H_2NSO_2Cl

c: $NH_2NH_2 \cdot H_2O$, KOH / DIETHYLENE GLYCOL

d: NaH / DMF, ≈ Br

e: N, N-DIETHYLANILINE, Δ

f: Pd/C, H_2

FIG. 38

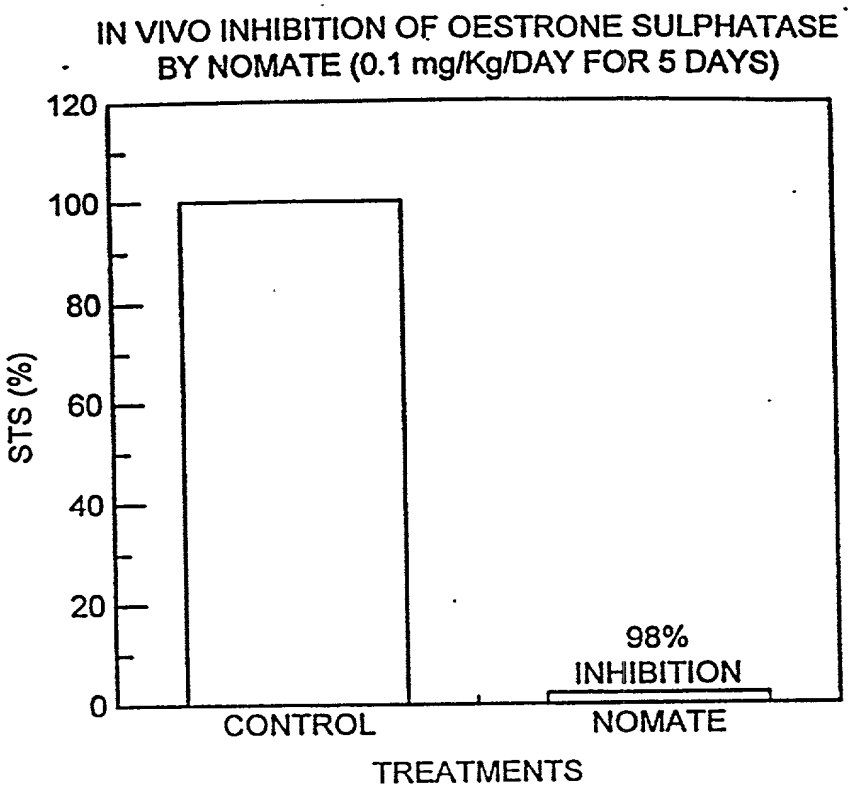

IN VIVO INHIBITION OF OESTRONE SULPHATASE BY NOMATE (0.1 mg/Kg/DAY FOR 5 DAYS)
120
100
80
60
40
20
0
STS (%)
98%
INHIBITION
CONTROL
NOMATE
TREATMENTS

FIG. 39

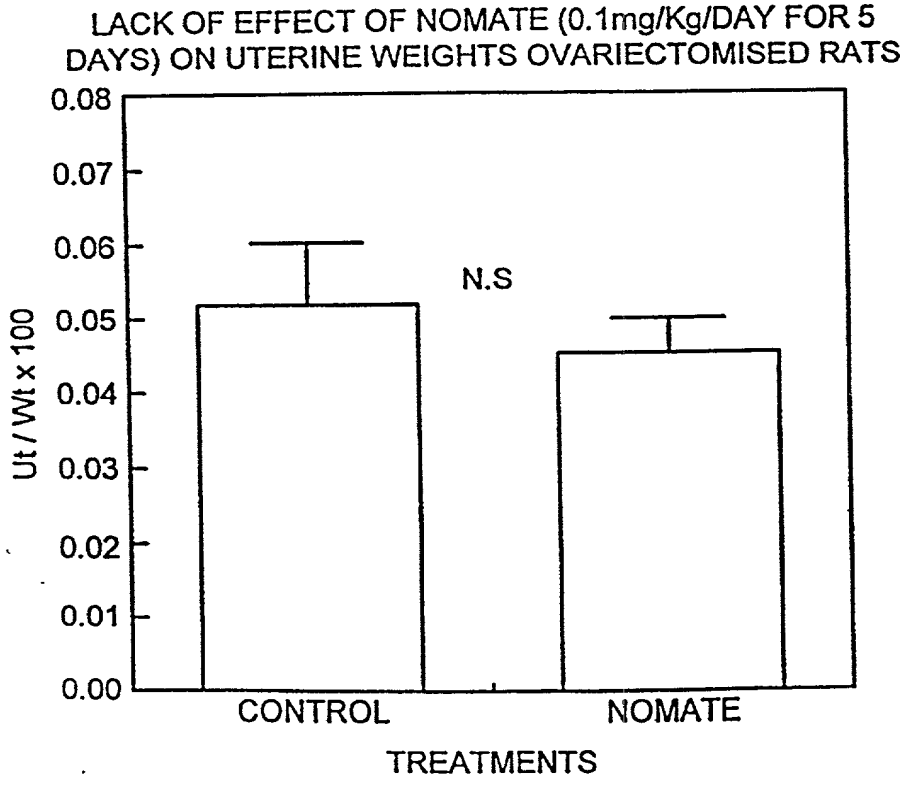

LACK OF EFFECT OF NOMATE (0.1mg/Kg/DAY FOR 5 DAYS) ON UTERINE WEIGHTS OVARIECTOMISED RATS
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
Ut / Wt x 100
N.S
CONTROL
NOMATE
TREATMENTS

FIG. 40